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Diseases of the Aorta The aorta is the conduit through which blood ejected from the left ventricle is delivered to the systemic arterial bed. In adults, its diameter is ~3.5 cm at the origin and in the ascending portion, ~2.5 cm in the descending portion in the thorax, and 1.8–2.0 cm in the abdomen. The aortic wall consists of a thin intima composed of endothelium, subendothelial connective tissue, and an internal elastic lamina; a thick tunica media composed of smooth muscle cells, elastic fibers, collagen, and extracellular matrix; and an adventitia composed primarily of connective tissue enclosing the vasa vasorum and nervi vascularis. In addition to the conduit function of the aorta, its viscoelastic and compliant properties serve a buffering function. The aorta is distended during systole to allow a portion of the stroke volume and elastic energy to be stored, and it recoils during diastole so that blood continues to flow to the periphery. Owing to its continuous exposure to high pulsatile pressure and shear stress, the aorta is particularly prone to injury and disease resulting from mechanical trauma. The aorta is also more prone to rupture than is any other vessel, especially with the development of aneurysmal dilation, since its wall tension, as governed by Laplace's law (i.e., proportional to the product of pressure and radius), will be increased. **CONGENITAL ANOMALIES OF THE AORTA** Congenital anomalies of the aorta usually involve the aortic arch and its branches. Symptoms such as dysphagia, stridor, and cough may

occur if an anomaly causes a ring around or otherwise compresses the esophagus or trachea. Anomalies associated with symptoms include double aortic arch, origin of the right subclavian artery distal to the left subclavian artery, and right-sided aortic arch with an aberrant left subclavian artery. A Kommerell diverticulum

is an anatomic remnant of a right aortic arch. Most congenital anomalies of the aorta do not cause symptoms and are detected during catheter-based procedures. The diagnosis of suspected congenital anomalies of the aorta typically is confirmed by computed tomographic (CT) or magnetic resonance (MR) angiography. Surgery is used to treat symptomatic anomalies.

CHAPTER 291 Coarctation of the aorta (Chap. 280) typically occurs near the insertion of the ligamentum arteriosum, adjacent to the left subclavian artery. It may be associated with a bicuspid aortic valve, aortic arch hypoplasia, other congenital heart defects, and intracranial aneurysms. A pulse delay or pressure differential between the upper and lower extremities should raise suspicion of aortic coarctation. Imaging modalities, including echocardiography, CT, and MR angiography are used to confirm the diagnosis. If untreated, hypertension develops in the arteries proximal to the coarctation. Treatment of hemodynamically significant aortic coarctation includes endovascular stent implantation if feasible or surgical repair.

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AORTIC ANEURYSM An aneurysm is defined as a pathologic dilation of a segment of a blood vessel. A true aneurysm involves all three layers of the vessel wall and is distinguished from a pseudoaneurysm, in which the intimal and medial layers are disrupted and the dilated segment of the aorta is lined by adventitia only and, at times, by perivascular clot. Aneurysms also may be classified according to their gross appearance. A fusiform aneurysm affects the entire circumference of a segment of the vessel, resulting in a diffusely dilated artery. In contrast, a saccular aneurysm involves only a portion of the circumference, resulting in an outpouching of the vessel wall. Aortic aneurysms also are classified according to location, i.e., abdominal versus thoracic. Aneurysms of the descending thoracic aorta are usually contiguous with infradiaphragmatic aneurysms and are referred to as thoracoabdominal aortic aneurysms.

■ ■ **ETIOLOGY** Aortic aneurysms result from conditions that cause degradation or abnormal production of the structural components of the aortic wall: elastin and collagen. The causes of aortic aneurysms may be broadly categorized as degenerative or sporadic, heritable, congenital, aortitis, infective, and trauma (Table 291-1). Inflammation, oxidative stress, proteolysis, and biomechanical wall stress contribute to the degenerative processes that characterize most aneurysms of the abdominal and descending thoracic aorta. These are mediated by B-cell and T-cell lymphocytes, macrophages, inflammatory cytokines, and matrix metalloproteinases that degrade elastin and collagen and alter the tensile strength and ability of the aorta to accommodate pulsatile stretch. The associated histopathology demonstrates destruction of elastin and collagen, decreased vascular smooth muscle, in-growth of new blood vessels, and inflammation. Factors associated with degenerative aortic aneurysms include aging, cigarette smoking, hypercholesterolemia, hypertension, and male sex. The most common pathologic condition associated with degenerative aortic aneurysms is atherosclerosis. Many patients with aortic aneurysms have coexisting risk factors for atherosclerosis, as well as atherosclerosis in other blood vessels. The pathologic condition of aortic aneurysms associated with genetic or developmental diseases is medial degeneration, a histopathologic term used to describe the degeneration of collagen and elastic fibers in the tunica media of the aorta as well as the loss of medial cells that are replaced by multiple clefts of mucoid material, such as proteoglycans. Medial degeneration characteristically affects the proximal aorta, results in

circumferential weakness and dilation, and leads to the development of fusiform aneurysms involving the ascending aorta and the sinuses of Valsalva. It is found in patients with Marfan syndrome, Loeys-Dietz syndrome, vascular Ehlers-Danlos syndrome (Chap. 425), hypertension, bicuspid aortic valves, Turner syndrome, and familial thoracic aortic aneurysm syndromes. It sometimes appears as an isolated condition in patients without any other apparent disease. Thoracic and abdominal aortic aneurysms also occur in patients with fibromuscular dysplasia, although the nature of the aortic pathology is not established.

TABLE 291-1 Diseases of the Aorta: Etiology and Associated Factors Aortic aneurysm

Degenerative/sporadic Cardiovascular System		Aging	Cigarette smoking	PART 6 Disorders of the	
Heritable		Hypercholesterolemia	Hypertension	Atherosclerosis	
Marfan syndrome		Loeys-Dietz syndrome	Ehlers-Danlos syndrome		
type IV		Aneurysm-osteoarthritis syndrome	Smooth muscle dysfunction syndrome		
Familial (nonsyndromic)		Congenital	Bicuspid aortic valve	Turner syndrome	
Aortic coarctation		Fibromuscular dysplasia	Chronic aortic dissection	Aortitis (see below)	
Infective (see below)		Trauma	Acute aortic syndromes (aortic dissection, acute intramural hematoma, penetrating atherosclerotic ulcer)		Degenerative disorders (see above)
Heritable/disorders (see above)		Congenital disorders (see above)		Hypertension	Aortitis
(see below)		Pregnancy	Trauma	Aortic occlusion	Thromboembolism
Aortitis	Vasculitis	Takayasu's arteritis		Giant cell arteritis	IgG4-related aortitis
Isolated aortitis		Rheumatic	Rheumatoid aortitis	HLA-B27-associated	
spondyloarthropathies		Behçet syndrome	Cogan syndrome	Infective	Syphilis
Tuberculosis		Mycotic (Salmonella, staphylococcal, streptococcal, fungal)			

Familial clusterings of aortic aneurysms occur in 20% of patients, suggesting a hereditary basis for the disease. Mutations of the gene that encodes fibrillin-1 are present in patients with Marfan syndrome. Fibrillin-1 is an important component of extracellular microfibrils, which support the architecture of elastic fibers and other connective tissue. Deficiency of fibrillin-1 in the extracellular matrix leads to excessive signaling by transforming growth factor β (TGF- β). Loeys-Dietz syndrome is caused by mutations in the genes that encode

TGF- β isoforms (TGFB2 and TGFB3), TGF- β receptors 1 (TGFR1) and 2 (TGFR2), and SMAD3, which encodes a downstream signaling protein involved with TGF binding to its receptors. Increased signaling by TGF- β and mutations of TGFR1, TGFR2, as well as TGFB2 and TGFB3, may cause thoracic aortic aneurysms. Thoracic aortic aneurysm is associated with autosomal dominant polycystic kidney disease, which is caused by mutations in PKD1. Mutations of the genes encoding the smooth muscle-specific alpha-actin (ACTA2), smooth muscle cell-specific myosin heavy chain 11 (MYH11), myosin light chain kinase (MYLK), and type I cGMP-dependent protein kinase (PRKG1), as well as mutations of TGFR2 and SMAD3 and several other pathogenic variants, have been reported in some patients with nonsyndromic familial thoracic aortic aneurysms. Mutations in type III procollagen (COL3A1) have been implicated in vascular Ehlers-Danlos syndrome. The infectious causes of aortic aneurysms include syphilis, tuberculosis, and other bacterial infections. Syphilis (Chap. 187) is a relatively uncommon cause of aortic aneurysm. Syphilitic periaortitis and meso aortitis damage elastic fibers, resulting in thickening and weakening of the aortic wall. Approximately 90% of syphilitic aneurysms are located in the ascending aorta or aortic arch. Tuberculous aneurysms (Chap. 183) typically affect the thoracic aorta and result from direct extension of infection from hilar lymph nodes or contiguous abscesses as well as from

bacterial seeding. Loss of aortic wall elasticity results from granulomatous destruction of the medial layer. A mycotic aneurysm is a rare condition that develops as a result of staphylococcal, streptococcal, *Salmonella*, or other bacterial or fungal infections of the aorta, usually at an atherosclerotic plaque. These aneurysms are usually saccular. Blood cultures are often positive and reveal the nature of the infective agent. Vasculitides associated with aortic aneurysm include Takayasu arteritis and giant cell arteritis, which may cause aneurysms of the aortic arch and descending thoracic aorta. Thoracic and abdominal aortic aneurysms also occur in patients with IgG4-related systemic disease or those with isolated aortitis. Spondyloarthropathies such as ankylosing spondylitis, rheumatoid arthritis, psoriatic arthritis, relapsing polychondritis, and reactive arthritis are associated with dilation of the ascending aorta. Aortic aneurysms also occur in patients with Behçet syndrome (Chap. 376) and Cogan syndrome. Traumatic aneurysms may occur after penetrating or nonpenetrating chest trauma and most commonly affect the descending thoracic aorta just beyond the site of insertion of the ligamentum arteriosum. Chronic aortic dissections are associated with weakening of the aortic wall that may lead to the development of aneurysmal dilatation.

■ ■ **THORACIC AORTIC ANEURYSMS** A contemporary definition of an aneurysm affecting the aortic root and ascending aorta is that of the diameter ≥ 4.5 cm, whereas a diameter of 4.0 cm to 4.4 cm is defined as aortic dilation. An aneurysm of the descending thoracic aorta and abdominal aorta is designated when their diameters are dilated 50% more than the adjacent normal diameter. The clinical manifestations and natural history of thoracic aortic aneurysms depend on their cause and location. Medial degeneration is the most common pathology associated with ascending aortic aneurysms, whereas atherosclerosis is the condition most frequently associated with aneurysms of the descending thoracic aorta. The average growth rate of thoracic aortic aneurysms is 0.1–0.2 cm per year. The risk of rupture is related to the size of the aneurysm and the presence of symptoms, ranging approximately from 2–3% per year for thoracic aortic aneurysms <4.0 cm in diameter to 7% per year for those >6 cm in diameter. Thoracic aortic aneurysms associated with Marfan syndrome may expand at a greater rate. Some patients with Loeys-Dietz syndrome, such as those with the TGFBR1 and TGFBR2 pathogenic variants and some with nonsyndromic familial thoracic aortic disease, are at greater risk of rupture at smaller aortic root sizes than those with Marfan syndrome. Most thoracic aortic aneurysms are asymptomatic; however, compression or erosion of adjacent tissue by aneurysms may cause symptoms such as chest pain, shortness of breath, cough, hoarseness, and dysphagia. Aneurysmal dilation of the ascending aorta may cause congestive heart failure as a consequence of aortic regurgitation,

FIGURE 291-1 A chest x-ray of a patient with a thoracic aortic aneurysm. and compression of the superior vena cava may produce congestion of the head, neck, and upper extremities. A chest x-ray may be the first test that suggests the diagnosis of a thoracic aortic aneurysm (Fig. 291-1). Findings include widening of the mediastinal shadow and displacement or compression of the trachea or left main stem bronchus. Echocardiography, particularly transesophageal echocardiography, can be used to assess the proximal ascending aorta and descending thoracic aorta. Contrast-enhanced CT, magnetic resonance imaging (MRI), and conventional invasive aortography are sensitive and specific tests for assessment of aneurysms of the thoracic aorta and involvement of branch vessels (Fig. 291-2). In asymptomatic patients whose aneurysms are too small to justify surgery, noninvasive testing with either contrast-enhanced CT or MRI should be performed initially at least every 6–12 months to monitor expansion. Subsequent surveillance imaging should be performed every 6–24 months depending on the size, stability of prior measurements, and the underlying cause. **FIGURE 291-2** A magnetic resonance angiogram demonstrating a

fusiform aneurysm of the ascending thoracic aorta. (Courtesy of Dr. Michael Steigner, Brigham and Women's Hospital, Boston, MA, with permission.)

Genetic testing is recommended in patients with ascending thoracic aortic disease who have features of Marfan syndrome, Loeys-Dietz syndrome, or vascular Ehlers-Danlos syndrome, or who present when they are <60 years of age.

CHAPTER 291 TREATMENT Thoracic Aortic Aneurysms Many of the treatment recommendations herein are derived from the recent American Heart Association (AHA)/American College of Cardiology (ACC) Aortic Disease Clinical Practice Guidelines. Treatment with either a β -adrenergic blocker or angiotensin receptor antagonist currently is recommended for patients with thoracic aortic aneurysms associated with Marfan syndrome and Loeys-Dietz syndrome who have evidence of aortic root dilatation to reduce the rate of further expansion. Clinical outcome trials have found that the rate of aortic root enlargement in patients with Marfan syndrome was similar with a β -adrenergic blocker, such as atenolol, and an angiotensin receptor antagonist, such as losartan. These classes of drugs likely confer beneficial effects by different mechanisms. β -adrenergic blockers may decrease the rate of aortic dilation in these patients by reducing stiffness, and angiotensin receptor antagonists may reduce the rate of aortic dilation by blocking TGF- β signaling. Combination therapy with both a β -adrenergic blocker and angiotensin receptor antagonist may be considered. In patients with Ehlers-Danlos syndrome, celiprolol, a β -adrenergic blocker with vasodilator properties, has shown efficacy, but is not available in the United States. For these and other patients with thoracic aortic aneurysms, additional medical therapy should be given as necessary to control hypertension. Risk factor modification with lipid-lowering therapy, smoking cessation interventions, as well as low-dose aspirin, is advised for patients with degenerative thoracic aortic aneurysms associated with atherosclerosis. Operative repair with placement of a prosthetic graft is indicated in patients with symptomatic ascending thoracic aortic aneurysms, and for most asymptomatic aneurysms, including those associated with bicuspid aortic valves, when the aortic root or ascending aortic diameter is ≥ 5.0 to ≥ 5.5 cm. The lower threshold applies to patients with high-risk features, such as a family history of aortic dissection or an aortic growth rate ≥ 0.3 cm per year for 2 years or when the growth rate is >0.5 cm per year, and when performed under the direction of an experienced multidisciplinary aortic team. Replacement of the ascending aorta ≥ 4.5 cm is reasonable in patients with bicuspid aortic valves undergoing aortic valve replacement because of severe aortic stenosis or aortic regurgitation. In patients with Marfan syndrome, aortic root and ascending thoracic aortic aneurysms of ≥ 4.5 to ≥ 5.0 cm should be considered for surgery, with the threshold also depending on the presence of high-risk features. Due to the higher risk of dissection at smaller aortic sizes in patients with Loeys-Dietz syndrome and those with nonsyndromic familial thoracic aortic aneurysms, the aortic diameter threshold for operative repair ranges from ≥ 4.0 to ≥ 5.0 cm, depending on the genetic variant and presence of high-risk features. Repair is indicated for patients with isolated aortic arch aneurysms and descending thoracic aortic aneurysms when the diameter is ≥ 5.5 cm. The threshold for repair of a descending thoracic aortic aneurysm of ≥ 5.0 cm may be considered in patients with syndromic and nonsyndromic heritable aortopathies or when the diameter of a descending thoracic aortic aneurysm has increased >0.5 cm per year.

Diseases of the Aorta ■ ■ ABDOMINAL AORTIC ANEURYSMS Abdominal aortic aneurysms occur more frequently in males than in females, and the incidence increases with age. Cigarette smoking is a potent modifiable risk factor. Abdominal aortic aneurysms ≥ 4.0 cm may affect 1–2% of men aged >50 years. At least 90% of all abdominal aortic

aneurysms >4.0 cm are related to atherosclerotic disease, and most of these aneurysms are below the level of the renal arteries.

PART 6 Disorders of the Cardiovascular System **A FIGURE 291-3** A computed tomographic angiogram depicting a fusiform abdominal aortic aneurysm before (A) and after (B) treatment with a bifurcated stent graft. (Courtesy of Drs. Elizabeth George and Frank Rybicki, Brigham and Women's Hospital, Boston, MA, with permission.) Prognosis is related to both the size of the aneurysm and the severity of coexisting coronary artery and cerebrovascular disease. The risk of rupture increases with the size of the aneurysm: the 5-year risk for aneurysms <5 cm is 1–2%, whereas it is 20–40% for aneurysms >5 cm in diameter. The formation of mural thrombi within aneurysms may predispose to peripheral embolization. An abdominal aortic aneurysm commonly produces no symptoms. It usually is detected on routine examination as a palpable, pulsatile, expansile, and nontender mass, or it is an incidental finding observed on an abdominal imaging study performed for other reasons. As abdominal aortic aneurysms expand, however, they may become painful. Some patients complain of strong pulsations in the abdomen; others experience pain in the chest, lower back, or scrotum. Aneurysmal pain is usually a harbinger of rupture and represents a medical emergency. More often, acute rupture occurs without any prior warning, and this complication is always life-threatening. Rarely, there is leakage of the aneurysm with severe pain and tenderness. Acute pain and hypotension occur with rupture of the aneurysm, which requires an emergency operation or endovascular repair. Abdominal radiography may demonstrate the calcified outline of the aneurysm; however, ~25% of aneurysms are not calcified and cannot be visualized by x-ray imaging. An abdominal ultrasound can delineate the transverse and longitudinal dimensions of an abdominal aortic aneurysm and may detect mural thrombus. Abdominal ultrasound is useful for serial documentation of aneurysm size and can be used to screen patients at risk for developing an aortic aneurysm. In a large study, ultrasound screening of men aged 65–74 years was associated with a risk reduction in aneurysm-related death of 42%. In a meta-analysis of population-based randomized clinical trials, ultrasound screening of men aged 65 years or older was associated with a 35% risk reduction in aneurysm-related death over 12–15 years. According to the AHA/ACC Guidelines on Aortic Disease, screening by ultrasonography is recommended for men aged ≥65 years who have ever smoked. Although the prevalence of abdominal aortic aneurysms is less in women than in men, the risk of abdominal aortic aneurysms is still substantially increased in women who have smoked. Accordingly, it is reasonable to consider abdominal aortic aneurysm screening in women aged ≥65 years who have ever smoked. In addition, screening for abdominal aortic aneurysms is recommended for males and

B females ≥65 years who have siblings or offspring with abdominal aortic aneurysms. Individuals with thoracic aortic or peripheral arterial aneurysms should also undergo screening for abdominal aortic aneurysms. CT with contrast and MRI are accurate noninvasive tests to determine the location and size of abdominal aortic aneurysms and to plan endovascular or open surgical repair (Fig. 291-3A). Contrast aortography may be used for the evaluation of patients with aneurysms, but the procedure carries a small risk of complications such as bleeding, allergic reactions, and atheroembolism. Since the presence of mural thrombi may reduce the luminal size, aortography may underestimate the diameter of an aneurysm. **TREATMENT Abdominal Aortic Aneurysms** Many of the treatment recommendations for abdominal aortic aneurysms are derived from the AHA/ACC Aortic Disease Practice Guidelines. Statins are indicated to reduce the risk of cardiovascular events related to atherosclerosis. Medical therapies, such as β-adrenergic blockers and renin-angiotensin

inhibitors, have not proven effective in reducing the rate of aneurysm growth. Nonetheless, antihypertensive therapy to lower the blood pressure to $<130/80$ mmHg is recommended to reduce the risk of adverse cardiovascular events. Similarly, antiplatelet agents, such as aspirin, are recommended in patients with abdominal aortic aneurysms to reduce the risk of adverse cardiovascular outcomes, but their effects on abdominal aortic aneurysm-specific outcomes are not established. Operative repair of the aneurysm with insertion of a prosthetic graft or endovascular placement of an aortic stent graft (Fig. 291-3B) is indicated for abdominal aortic aneurysms of any size that are expanding rapidly or are associated with symptoms. For asymptomatic aneurysms, abdominal aortic aneurysm repair is indicated if the diameter is ≥ 5.5 cm in men and ≥ 5.0 cm in women. In randomized trials of patients with abdominal aortic aneurysms <5.5 cm, there was no difference in the long-term (>8 -year) mortality rate between those followed with ultrasound surveillance and those undergoing elective endovascular or surgical repair. The risk of rupture, however, was higher in women than in men at smaller diameters. Thus, serial noninvasive follow-up of smaller aneurysms

(<5.5 cm in men and <5.0 cm in women) is an alternative to immediate repair. The decision to perform an open surgical operation or endovascular repair is based in part on the vascular anatomy and comorbid conditions. Endovascular repair of abdominal aortic aneurysms has a lower short-term morbidity rate but a comparable long-term mortality rate with open surgical reconstruction. Long-term surveillance with CT or MR aortography is indicated after endovascular repair to detect leaks and possible aneurysm expansion. In surgical candidates, careful preoperative cardiac and general medical evaluations (followed by appropriate therapy for complicating conditions) are essential. Preexisting coronary artery disease, congestive heart failure, pulmonary disease, diabetes mellitus, and advanced age add to the risk of surgery. With careful preoperative cardiac evaluation and postoperative care, the operative mortality rate approximates 1–2%. After acute rupture, the mortality rate of emergent operation is 45–50%. Endovascular repair with stent placement is an alternative approach to treat ruptured aneurysms and may be associated with a lower mortality rate.

ACUTE AORTIC SYNDROMES

The four major acute aortic syndromes are aortic rupture (discussed earlier), aortic dissection, intramural hematoma, and penetrating atherosclerotic ulcer. Aortic dissection is caused by a tear of the intima. It often occurs along the right lateral wall of the ascending aorta where the hydraulic shear stress is high. Another common site is the descending thoracic aorta just below the ligamentum arteriosum. The initiating event is either a primary intimal tear with secondary dissection into the media or a medial hemorrhage that dissects into and disrupts the intima. The pulsatile aortic flow then dissects along the elastic lamellar plates of the aorta and creates a false lumen. The dissection usually propagates distally down the descending aorta and into its major branches, but it may propagate proximally. Distal propagation may be limited by atherosclerotic plaque. In some cases, a secondary distal intimal disruption occurs, resulting in the reentry of blood from the false to the true lumen. There are at least two important pathologic and radiologic variants of aortic dissection: intramural hematoma without an intimal flap and penetrating atherosclerotic ulcer. Acute intramural hematoma is thought to result from rupture of the vasa vasorum with hemorrhage into the wall of the aorta. Most of these hematomas occur in the descending thoracic aorta. Acute intramural hematomas may progress to dissection and rupture. Penetrating atherosclerotic ulcers are caused by erosion of a plaque into the aortic media, are usually localized, but may evolve into an intramural hematoma and also progress to dissection and rupture. They are found primarily in the middle and distal portions of the descending thoracic aorta and are associated with

extensive atherosclerotic disease. The ulcer can erode beyond the internal elastic lamina, leading to medial hematoma, and may progress to false aneurysm formation or rupture. Several classification schemes have been developed for thoracic aortic dissections. DeBakey and colleagues initially classified aortic dissections as type I, in which an intimal tear occurs in the ascending aorta but the dissection may propagate to the aortic arch, the descending thoracic aorta, and even the abdominal aorta; type II, in which the dissection is limited to the ascending aorta; and type III, in which the intimal tear is located in the descending aorta with distal propagation of the dissection (Fig. 291-4). Another classification (Stanford) is that of type A, in which the dissection involves the ascending aorta (proximal dissection), and type B, in which it is limited to the arch and/or descending aorta (distal dissection). From a management standpoint, classification of aortic dissections and intramural hematomas into type A or B is more practical and useful, since DeBakey types I and II are managed in a similar manner. The factors that predispose to aortic dissection include those associated with medial degeneration and others that increase aortic wall stress (Table 291-1). Systemic hypertension is a coexisting condition in 70% of patients. Aortic dissection is the major cause of morbidity and

Type A CHAPTER 291 Diseases of the Aorta Type B FIGURE 291-4 Classification of aortic dissections. Stanford classification: Type A dissections (top) involve the ascending aorta independent of site of tear and distal extension; type B dissections (bottom) involve transverse and/or descending aorta without involvement of the ascending aorta. DeBakey classification: Type I dissection involves ascending to descending aorta (top left); type II dissection is limited to ascending or transverse aorta, without descending aorta (top center + top right); type III dissection involves descending aorta only (bottom left). (Reproduced with permission from DC Miller, in RM Doroghazi, EE Slater [eds]: Aortic Dissection. New York, McGraw-Hill, 1983.) mortality in patients with Marfan syndrome (Chap. 425) or Loeys-Dietz syndrome, and similarly may affect patients with Ehlers-Danlos syndrome. The incidence also is increased in patients with inflammatory aortitis (i.e., Takayasu's arteritis, giant cell arteritis), congenital aortic valve anomalies (e.g., bicuspid valve), coarctation of the aorta, and a history of aortic trauma. In addition, the risk of dissection is increased in otherwise normal women during the third trimester of pregnancy. Aortic dissection also may occur as a consequence of weightlifting, cocaine use, or deceleration injury. ■ ■ CLINICAL MANIFESTATIONS The peak incidence of aortic dissection is in the sixth and seventh decades. Men are more affected than women by a ratio of 2:1. The presentations of aortic dissection and its variants are the consequences of intimal tear, dissecting hematoma, occlusion of involved arteries, and compression of adjacent tissues. Acute aortic dissection presents with the sudden onset of pain (Chap. 15), which often is described as very severe and tearing and is associated with diaphoresis. The pain may be localized to the front or back of the chest, often the interscapular region, and typically migrates with propagation of the dissection. Other symptoms include syncope, dyspnea, and weakness. Physical findings may include hypertension or hypotension, loss of pulses, aortic regurgitation, pulmonary edema, and neurologic findings due to carotid artery obstruction (hemiplegia, hemianesthesia) or spinal cord ischemia (paraplegia). Bowel ischemia, hematuria, and myocardial ischemia all may occur. These clinical manifestations reflect complications resulting from the dissection occluding the major arteries. Furthermore, clinical manifestations may result from the compression of adjacent structures (e.g., superior cervical ganglia, superior vena cava, bronchus, esophagus) by the expanding dissection causing aneurysmal dilation and include Horner's syndrome, superior vena cava syndrome, hoarseness, dysphagia, and airway compromise. Hemopericardium and cardiac tamponade may complicate a type A lesion with retrograde

dissection. Acute aortic regurgitation is an important and common (>50%) complication of proximal dissection. It is the outcome of either

a circumferential tear that widens the aortic root or a disruption of the annulus by a dissecting hematoma that tears a leaflet(s) or displaces it inferior to the line of closure. Signs of aortic regurgitation include bounding pulses, a wide pulse pressure, a diastolic murmur often radiating along the right sternal border, and evidence of congestive heart failure. The clinical manifestations depend on the severity of the regurgitation.

PART 6 Disorders of the Cardiovascular System In dissections involving the ascending aorta, the chest x-ray often reveals a widened superior mediastinum. A pleural effusion (usually left-sided) also may be present. This effusion is typically serosanguineous and not indicative of rupture unless accompanied by hypotension and falling hematocrit. In dissections of the descending thoracic aorta, a widened mediastinum may be observed on chest x-ray. In addition, the descending aorta may appear to be wider than the ascending portion. An electrocardiogram that shows no evidence of myocardial ischemia is helpful in distinguishing aortic dissection from myocardial infarction among patients who present with chest pain. Rarely, the dissection involves the right or, less commonly, left coronary ostium and causes acute myocardial infarction. The diagnosis of aortic dissection can be established by noninvasive techniques such as echocardiography, CT, and MRI. Aortography is used less commonly because of the accuracy of these noninvasive techniques. Transthoracic echocardiography can be performed simply and rapidly and has an overall sensitivity of 60–85% for aortic dissection. For diagnosing proximal ascending aortic dissections, its sensitivity exceeds 80%; it is less useful for detecting dissection of the arch and descending thoracic aorta. Transesophageal echocardiography requires greater skill and patient cooperation but is very accurate in identifying dissections of the ascending and descending thoracic aorta but not the arch, achieving 98% sensitivity and ~90% specificity. Echocardiography also provides important information regarding the presence and severity of aortic regurgitation and pericardial effusion. CT and MRI are both highly accurate in identifying the intimal flap and the extent of the dissection and involvement of major arteries; each has a sensitivity and specificity >90%. They are useful in recognizing intramural hemorrhage and penetrating ulcers. The relative utility of CT, MRI, and transesophageal echocardiography depends on the availability and expertise in individual institutions, although among these, CT is the imaging method most often used due to the presence of CT scanners near emergency rooms and the rapidity of performance.

TREATMENT Aortic Dissection Medical therapy should be initiated as soon as the diagnosis is considered. The patient should be admitted to an intensive care unit for hemodynamic monitoring. Unless hypotension is present, therapy should be aimed at reducing cardiac contractility and systemic arterial pressure, and thus shear stress. For acute dissection, unless contraindicated, β -adrenergic blockers should be administered parenterally, using intravenous propranolol, metoprolol, or the short-acting esmolol to achieve a heart rate of 60–80 beats/min. This should be accompanied by intravenous dilators, such as sodium nitroprusside, if needed to lower systolic blood pressure to ≤ 120 mmHg. Labetalol (Chap. 288), a drug with both β - and α -adrenergic blocking properties, also may be used as a parenteral agent in acute therapy for dissection. The calcium channel antagonists verapamil and diltiazem may be used intravenously if nitroprusside or β -adrenergic blockers can not be employed. The addition of a parenteral angiotensin-converting enzyme (ACE) inhibitor such as enalaprilat to a β -adrenergic blocker also may be considered. Isolated use of a direct vasodilator such as hydralazine is contraindicated because these agents can increase hydraulic shear and

heart rate and may propagate the dissection. Emergent or urgent surgical correction is the preferred treatment for acute ascending aortic dissections and intramural hematomas (type A). Surgery involves excision of the intimal flap, obliteration of the false lumen, and placement of an interposition graft. Aortic

valve repair or aortic root replacement with a composite valvegraft conduit is used if the aortic valve is disrupted. The overall in-hospital mortality rate after surgical treatment of patients with aortic dissection is reported to be 15–25%. The major causes of perioperative mortality and morbidity include myocardial infarction, paraplegia, renal failure, tamponade, hemorrhage, and sepsis. Thoracic endovascular aortic repair with an endoluminal stent graft is indicated for complicated type B dissections, including those characterized by propagation, compromise of major aortic branches, impending rupture, or continued pain. Other transcatheter techniques, such as fenestration of the intimal flaps and stenting of narrowed branch vessels to increase flow to compromised organs, are used in selected patients. Surgical correction is indicated for complicated type B dissections, particularly if endovascular repair is not feasible. Hybrid procedures consisting of both surgery and endovascular repair may be used when the dissection involves both the aortic arch and the descending thoracic aorta. For uncomplicated and stable distal dissections and intramural hematomas (type B), medical therapy is the preferred treatment. The in-hospital mortality rate of medically treated patients with type B dissection is ~12%. Long-term therapy for patients with aortic dissection and intramural hematomas (with or without surgery) consists of control of hypertension and reduction of cardiac contractility with the use of β -adrenergic blockers plus other antihypertensive agents, such as ACE inhibitors or calcium antagonists. Patients with chronic type B dissection and intramural hematomas should be followed on an outpatient basis initially at 1 month, 6 months, and 12 months, and then, if stable, every 12 months with contrast-enhanced CT or MRI to detect propagation or expansion. Patients with Marfan syndrome are at high risk for postdissection complications. The long-term prognosis following hospital discharge for patients with treated dissections is generally good with careful follow-up; the 10-year survival rate is ~60%. ■ ■

CHRONIC ATHEROSCLEROTIC OCCLUSIVE DISEASE Atherosclerosis may affect the thoracic and abdominal aorta. Occlusive aortic disease caused by atherosclerosis usually is confined to the distal abdominal aorta below the renal arteries. Frequently the disease extends to the iliac arteries (Chap. 292). Claudication characteristically involves the buttocks, thighs, and calves and may be associated with impotence in males (Leriche syndrome). The severity of the symptoms depends on the adequacy of collaterals. With sufficient collateral blood flow, a complete occlusion of the abdominal aorta may occur without the development of ischemic symptoms. The physical findings include the absence of femoral and other distal pulses bilaterally and the detection of an audible bruit over the abdomen (usually at or below the umbilicus) and the common femoral arteries. Atrophic skin, loss of hair, and coolness of the lower extremities usually are observed. In advanced ischemia, rubor on dependency and pallor on elevation can be seen. The diagnosis usually is established by physical examination and noninvasive testing, including leg pressure measurements, Doppler velocity analysis, pulse volume recordings, and duplex ultrasonography. The anatomy may be defined by MRI, CT, or conventional contrast angiography, typically performed when one is considering revascularization. Catheter-based endovascular or operative treatment is indicated in patients with lifestyle-limiting or debilitating symptoms of claudication and patients with chronic limb-threatening ischemia. ■ ■

ACUTE AORTIC OCCLUSION Acute occlusion in the distal abdominal aorta constitutes a medical emergency because it threatens the viability of the lower extremities; it usually results from an occlusive (saddle)

embolus that almost always originates from the heart. Rarely, acute occlusion may occur as the result of in situ thrombosis in a preexisting severely narrowed segment of the aorta. The clinical picture is one of acute ischemia of the lower extremities. Severe rest pain, coolness, and pallor of the lower extremities and the absence of distal pulses bilaterally are the usual manifestations.

Diagnosis should be established rapidly by MRI, CT, or aortography. Emergency thrombectomy or revascularization is indicated.

AORTITIS Aortitis, a term referring to inflammatory disease of the aorta, may be caused by large vessel vasculitides such as Takayasu arteritis, giant cell arteritis, IgG4-related systemic disease, isolated aortitis, rheumatic and HLA-B27-associated spondyloarthropathies, Behçet syndrome, antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides, Cogan syndrome, Erdheim-Chester disease, and infections such as syphilis, tuberculosis, and Salmonella, or it may be associated with retroperitoneal fibrosis. Aortitis may result in aneurysmal dilation and aortic regurgitation, occlusion of the aorta and its branch vessels, or acute aortic syndromes.

■ **TAKAYASU ARTERITIS** (See also Chap. 375) This inflammatory disease often affects the ascending aorta and aortic arch, causing obstruction of the aorta and its major arteries. Takayasu arteritis is also termed pulseless disease because of the frequent occlusion of the large arteries originating from the aorta. It also may involve the descending thoracic and abdominal aorta and occlude large branches such as the renal arteries. Aortic aneurysms also may occur. The pathology is a panarteritis characterized by mononuclear cells and occasionally giant cells, with marked intimal hyperplasia, medial and adventitial thickening, and, in the chronic form, fibrotic occlusion. The disease is most prevalent in young females of Asian descent but does occur in women of other geographic and ethnic origins and also in young men. During the acute stage, fever, malaise, weight loss, and other systemic symptoms may be evident. Elevations of the erythrocyte sedimentation rate and C-reactive protein are common. The chronic stages of the disease, which is intermittently active, present with symptoms related to large artery occlusion, such as upper extremity claudication, cerebral ischemia, and syncope. The process is progressive, and there is no definitive therapy. Glucocorticoids are effective in most patients during the acute phase. Other immunosuppressive agents, such as methotrexate, azathioprine, leflunomide, or mycophenolate, are prescribed to some patients to lower glucocorticoid requirements and treat relapses. Biologically targeted agents, such as the tumor necrosis factor (TNF) inhibitors etanercept and infliximab, are also used, but efficacy has not been established in randomized clinical trials. Surgical bypass or endovascular intervention of a critically stenotic artery may be necessary.

■ **GIANT CELL ARTERITIS** (See also Chap. 375) This vasculitis occurs in older individuals and affects women more often than men. Primarily large and medium-size arteries are affected. The pathology is that of focal granulomatous lesions involving the entire arterial wall; it frequently is associated with polymyalgia rheumatica. Obstruction of medium-size arteries (e.g., temporal and ophthalmic arteries) and major branches of the aorta and the development of aortitis and aortic regurgitation are important complications of the disease. High-dose glucocorticoid therapy should be administered early and then gradually tapered. Immunosuppressive therapy with methotrexate may allow reduction in steroid dosage and reduce the risk of relapse. Tocilizumab, an interleukin-6 antagonist, demonstrated efficacy in several randomized trials. Other biologically targeted therapies are under investigation.

■ **IGG4-RELATED AORTITIS** Aortitis may occur in patients with IgG4-related disease (Chap. 380) and is associated with retroperitoneal fibrosis and hydronephrosis. It can affect the thoracic and abdominal aorta, as well as the iliac arteries. Serum IgG4 levels may be elevated but are not diagnostic. Histopathologic characteristics include a lymphoplasmacytic infiltrate that comprises IgG4-positive plasma cells, fibrosis, and

obliterative adventitial phlebitis; it affects men more than women and typically occurs in middle age. Glucocorticoids are used for initial treatment. Case series have reported efficacy with rituximab, an anti-CD20 monoclonal antibody. Immunosuppressive agents such as azathioprine are steroid sparing and may be effective.

■ ■ ISOLATED AORTITIS Isolated abdominal aortitis is characterized by adventitial and periaortic inflammation with thickening of the aortic wall; it is associated with abdominal aortic aneurysms and idiopathic retroperitoneal fibrosis. Affected individuals may present with vague constitutional symptoms, fever, and abdominal pain. Retroperitoneal fibrosis can cause ureteral obstruction and hydronephrosis. Glucocorticoids and immunosuppressive agents may reduce the inflammation.

CHAPTER 291 ■ ■ RHEUMATIC AORTITIS Rheumatoid arthritis (Chap. 370), ankylosing spondylitis (Chap. 374), psoriatic arthritis (Chap. 374), reactive arthritis (formerly known as Reiter's syndrome) (Chap. 374), relapsing polychondritis, and inflammatory bowel disorders may all be associated with aortitis involving the ascending aorta. The inflammatory lesions usually involve the ascending aorta and may extend to the sinuses of Valsalva, the mitral valve leaflets, and adjacent myocardium. The clinical manifestations are aneurysm, aortic regurgitation, and involvement of the cardiac conduction system. Diseases of the Aorta ■ ■ INFECTIVE AORTITIS Infective aortitis may result from direct invasion of the aortic wall by bacterial pathogens such as *Staphylococcus*, *Streptococcus*, and *Salmonella* or by fungi. These bacteria cause aortitis by infecting the aorta at sites of atherosclerotic plaque. Bacterial proteases lead to degradation of collagen, and the ensuing destruction of the aortic wall leads to the formation of a saccular aneurysm referred to as a mycotic aneurysm. Mycotic aneurysms have a predilection for the suprarenal abdominal aorta. The pathologic characteristics of the aortic wall include acute and chronic inflammation, abscesses, hemorrhage, and necrosis. Mycotic aneurysms typically affect the elderly and occur in men three times more frequently than in women. Patients may present with fever, sepsis, and chest, back, or abdominal pain; there may have been a preceding diarrheal illness. Blood cultures are positive in the majority of patients. Both CT and MRI are useful to diagnose mycotic aneurysms. Treatment includes antibiotic therapy and surgical removal of the affected part of the aorta and revascularization of the lower extremities with grafts placed in uninfected tissue. Syphilitic aortitis is a late manifestation of luetic infection (Chap. 187) that usually affects the proximal ascending aorta, particularly the aortic root, resulting in aortic dilation and aneurysm formation. Syphilitic aortitis occasionally may involve the aortic arch or the descending aorta. The aneurysms may be saccular or fusiform and are usually asymptomatic, but compression of and erosion into adjacent structures may result in symptoms; rupture also may occur. The initial lesion is an obliterative endarteritis of the vasa vasorum, especially in the adventitia. This is an inflammatory response to the invasion of the adventitia by the spirochetes. Destruction of the aortic media occurs as the spirochetes spread into this layer, usually via the lymphatics accompanying the vasa vasorum. Destruction of collagen and elastic tissues leads to dilation of the aorta, scar formation, and calcification. These changes account for the characteristic radiographic appearance of linear calcification of the ascending aorta. The disease typically presents as an incidental chest radiographic finding 15–30 years after initial infection. Symptoms may result from aortic regurgitation, narrowing of coronary ostia due to syphilitic aortitis, compression of adjacent structures (e.g., esophagus), or rupture. Diagnosis is established by a positive serologic test, such as rapid plasmin reagin (RPR), Venereal Disease Research Laboratory (VDRL), or fluorescent treponemal antibody absorption (FTA-ABS). Treatment includes penicillin and surgical excision and repair. ■ ■ FURTHER READING Chou E et al: Genetics and mechanisms of thoracic aortic disease.

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Revision #1

Created 2026-01-06 16:33:59 UTC by Omar Ayman

Updated 2026-01-06 16:33:59 UTC by Omar Ayman